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Jay A. Goldstein

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Pabst Patent Group LLP

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1 RECORD OF ORAL HEARING
2 UNITED STATES PATENT AND TRADEMARK OFFICE

3
4 BEFORE THE BOARD OF PATENT APPEALS
5 AND INTERFERENCES

6 *Ex Parte* JAY GOLDSTEIN, MICHAEL ROTHMAN,
7 and WHE-YONG LO

8
9 Appeal 2010-006562
10 Application 10/691,928
Technology Center 1600

11
12 Oral Hearing Held: October 18, 2011

13
14 Before TONI R. SCHEINER, LORA M. GREEN, and STEPHEN WALSH,
15 *Administrative Patent Judges.*

16 APPEARANCES:

17 ON BEHALF OF THE APPELLANTS:

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22
23 The above-entitled matter came on for hearing on Tuesday,
24 October 18, 2011, commencing at 9:05 a.m., at the U.S. Patent and
25
26

1 Trademark Office, 600 Dulany Street, Alexandria, Virginia, before
2 Timothy J. Atkinson, Jr., a Notary Public.

3 THE USHER: Good morning. Calendar No. 17, Appeal No. 2010-
4 006562, Mr. Terapane.

5 JUDGE SCHEINER: Thank you. Good morning.

6 MR. TERAPANE: Good morning. How are you?

7 JUDGE SCHEINER: I'm fine, thanks. I just wanted to let you know
8 that Judge Walsh is joining us from an undisclosed location.

9 MR. TERAPANE: Location unknown? Okay, good morning.

10 JUDGE WALSH: Good morning.

11 JUDGE SCHEINER: Judge Walsh, we're going to start, whenever
12 you're ready.

13 MR. TERAPANE: Okay, thank you. My name is Michael Terapane;
14 I'm appearing on behalf of the applicants in this case, and with me today is
15 Dr. Jay Goldstein --

16 JUDGE SCHEINER: Good morning.

17 DR. GOLDSTEIN: Good morning.

18 MR. TERAPANE: -- who's an inventor on the application, and he's
19 going to speak briefly at the end.

20 JUDGE SCHEINER: May I just make sure that, Steve -- Judge
21 Walsh, can you hear us all right?

22 No. Can you hear what's going on in the hearing room? No.

23 JUDGE WALSH: Yes.

24 JUDGE SCHEINER: Yes.

25 MR. TERAPANE: Yes.

26 JUDGE SCHEINER: Okay.

1 MR. TERAPANE: Okay.

2 JUDGE SCHEINER: Can you hear Mr. Terapane?

3 JUDGE WALSH: Yes.

4 JUDGE SCHEINER: Okay.

5 MR. TERAPANE: Okay.

6 JUDGE SCHEINER: All right, now I'm probably going to -- I'm
7 supposed to push this button when I speak to you and turn it off when I
8 don't, so I think I'll probably mess that up a couple times because I'm not
9 used to it.

10 MR. TERAPANE: We'll work through it.

11 JUDGE SCHEINER: All right, signing off, okay.

12 MR. TERAPANE: Okay, thank you. So I think we'll just jump in
13 with the -- with the rejections that were set forth by the Examiner. I'll
14 address them in the order that they were presented.

15 The invention here is the discovery that you could combine with an
16 antifungal agent a low to low-medium potency steroid and have that
17 effectively treat topical fungal infections while avoiding side effects that
18 have been associated with high-potency formulations like Lotrisone, which
19 was the standard at the time.

20 So the first reference that was cited by the Examiner was the '056
21 patent to Quigley, and the first thing I want to point out in Quigley is, there
22 is a table at columns 4 and 5 which provides a list of various formulations of
23 different steroids. And something I want to point out in this table is, and it's
24 very important to keep this in mind, is that there are really at least, and really
25 three critical factors that determine potency of a steroid. The first is,
26 obviously, the drug itself. The second is the concentration, which is another

1 sort of obvious factor, but the third one is the way in which it's formulated,
2 and so creams are different than lotions, which are different than ointments.

3 And I think more to the point is, different creams can have different
4 potencies. So if you look in that table, for instance, there are three different
5 creams for betamethasone that actually are classified as I, II and III. So
6 there's lots of variability here in terms of what the potency ends up being,
7 based on how it's formulated, what the drug is, and what the concentration
8 is.

9 Now really, the specific rejection that the Examiner raised here, he
10 went right to Table G, which is in column 11, which is really a prophetic
11 example, it's sort of a representative prophetic example of how you can
12 make a lotion within the scope of this patent. It has general disclosure with
13 respect to the concentration range of the steroid; doesn't necessarily
14 reference a specific steroid that you would use.

15 The Examiner took that table, took .02 percent and said, well, if you
16 combine those things, you end up getting a .02 percent lotion, which is in the
17 table that I just referred to, classified as a low or medium potency steroid.
18 So there's a couple of issues with this.

19 The first off, is the disclosure in this reference is incredibly broad.
20 There's no disclosure here to specifically select a low or low-medium
21 potency steroid. So under the standard articulated by *In re Arkley*, by the
22 Court, where it said, you know, if it's so broad that you'd have to selectively
23 pick and choose to be able to get to something, that's not anticipatory. And
24 that's really what we have here, and the Examiner was forced to sort of pick
25 and choose from various parts of this to try to come up with something that
26 he thought anticipates the claims.

1 Not only in addition to that, but we don't even know that this lotion
2 formulation that's prophetically described here is, in fact, the same lotion
3 that's listed in the table. And as I just mentioned, because even the same
4 vehicles can have different potencies, so one cream could be more potent
5 than another cream or vice versa, we don't even know that the lotions would
6 have the same potency.

7 The Examiner also failed to recognize, I think, or at least to consider,
8 the working examples that follow these prophetic examples. So if you go to,
9 for example, example 10, which is actually a formulation that was prepared
10 within the patent, this is a lotion formulation. But notice that the potency of
11 betamethasone, which is the steroid that he focused on because it's described
12 as the preferred one in the patent, the concentration here is three times the
13 concentration of that low-potency lotion formulation that's described in the
14 table. And so this is going to be a much, much higher-potency formulation
15 than what the Examiner alleges is disclosed here.

16 And then finally, I just want to add, when you get past those working
17 formulation examples that were made and we actually get into some
18 examples that are comparing efficacy, and this is examples 12 and 13, what
19 they ultimately chose were creams that are high-potency formulations. And
20 so there's just -- there is no disclosure in this reference, either explicitly or
21 inherently, to choose a low to low-medium strength steroid formulation in
22 order to effectively treat fungal infection while avoiding side effects.

23 JUDGE WALSH: Mr. Terapane, I have one question about the
24 formulations that you just went through.

25 MR. TERAPANE: Sure.

26

1 JUDGE WALSH: Earlier in the Quigley patent, the Examiner had
2 directed attention to column 1 at around lines 28 to 32 or so.

3 MR. TERAPANE: Yes.

4 JUDGE WALSH: And it seems there that Quigley addresses at least
5 what seems to be a very similar problem as to one your inventors are
6 addressing. And then in column 2, at about line 25, Quigley says that and
7 then it shows their formulation delivers the antifungal agent and the steroid,
8 but it minimizes penetration of skin and avoids side effects. So what weight
9 should we give that part of the disclosure?

10 MR. TERAPANE: So, I think there's two things to keep in mind in
11 view of that disclosure. The first is I think it's telling that there's actually no
12 data in the patent with respect to side effects. There is data with respect to
13 efficacy in treating fungal infection, but we actually don't know that the
14 formulations they made and ultimately studied avoided side effects. I mean,
15 there's no data that, well, they did an irritation study or some other sort of
16 study to say that.

17 Secondly, we don't know in what context that statement is made with
18 respect to potency of the steroid formulation. In other words, if you look at
19 what was done ultimately in terms of the working examples that were done,
20 and really even in terms of most of the prophetic examples, the formulations
21 are all either mid-potency at a minimum, but more likely high-medium or
22 high-potency steroids. So I don't think there's a disclosure here, either
23 explicitly or inherently, of a low to low-medium steroid formulation which
24 effectively treats the fungal infection while avoiding side effects.

25 Remember, there's two things here: You got to avoid side effects, but
26 you also have to effectively treat the underlying fungal infection, or what's

1 the point? So I think these are general statements but they're not tied to
2 anything in particular in terms of potency of the steroid, but more to the
3 point, there's no data that, in fact, shows that they were able to even
4 accomplish avoiding side effects with respect to the working examples that
5 they have, which is really all we have to go on in terms of the potency of the
6 steroid that they're using.

7 The prophetic formulations are so broad that you literally would have
8 to pick and choose to get to even a low to low-medium like, which is what
9 we are claiming, and there's no evidence, in fact, that that was effective for
10 what they were looking at. So I would even argue I'm not sure they're --

11 JUDGE WALSH: Assuming --

12 MR. TERAPANE: I'm sorry, go ahead.

13 JUDGE WALSH: Assuming for the moment that we take your point
14 about picking and choosing, do you want to also address at this time the
15 portion of the quick disclosure that the Examiner referred us to at column 5?
16 And that was about line 55 or so. I mean, if you want to save this for --
17 discussion, that's fine too, but it seems to be related to what you were
18 saying.

19 MR. TERAPANE: No, I think we can address that here as well. I
20 mean, yeah, there's a general statement here that says if the potency is high
21 you can use a little bit less; if it's low, you can use a little bit more. I'm not
22 sure that's really a teaching of selecting a low to low-medium potency
23 steroid. I think what it's saying is is that if you started with a low, you
24 would increase the concentration, you'd increase the amount, which
25 ultimately means you would increase the potency.

26

1 And so I think if you look at that in the context of what's taught in the
2 prophetic and working examples, what you end up with is a formulation
3 which is, at the weakest, a mid strength, but more likely is actually a
4 medium-high to high potency formulation, and that's what they're looking
5 at.

6 And I think that's supported by the fact that if you look in the
7 examples too, their treatment times are fairly short. I mean, they claim that
8 they get basically 70 to 80 percent efficacy after 8 days. I mean, that's a
9 fairly short treatment period, so I think they're focused on, you know,
10 basically, a means of using a medium to medium-high or high potency
11 formulation, but being able to shorten duration of treatment time so that you
12 avoid side effects that might be associated with it.

13 There's no teaching because nobody recognized at the time that a low
14 to low-medium steroid formulation would, in fact, not only avoid side
15 effects; you might have guessed that that certainly may have been the case,
16 but you wouldn't have guessed it would have effectively treated the
17 underlying fungal infection as well.

18 And that does -- you're right, that does tie into the obvious, and matter
19 of fact, I can probably go over that relatively quickly when I get there,
20 because a lot of the same arguments will apply. Okay.

21 The second reference that was cited for anticipation was the Burnett
22 reference, and a couple of general -- well, not general, specific comments
23 here about this. The first thing to keep in mind is that Burnett teaches
24 anhydrous compositions, that is, those without water or very little water. In
25 sort of the terms of the art, that typically means an ointment; ointments are
26 typically topical formulations that don't contain water.

1 One of the things you will notice if you look in that table back in
2 Quigley that had some representative formulations and their potencies,
3 ointments are much, much higher potency than, say, formulations that
4 contain water, like creams or lotions. So clearly, the focus here is going to
5 be on a formulation that likely is at least medium if not medium-to-high
6 potency formulation by virtue of the fact that it's an ointment.

7 On top of that, it also includes a penetration enhancer which is going
8 to enhance penetration of the steroid into the skin. Matter of fact, they
9 actually talk about the fact that what they want to do here is, they want to
10 drive it into the dermis and the epidermis. They're trying to avoid getting
11 the steroid to a particular receptor to avoid systemic side effects, but in fact
12 what they're really trying to do is get it into the skin which is going to
13 actually increase the chances that you're going to have these adverse local
14 side effects that we, actually, specifically avoid in the claim language that
15 we have.

16 And so the Examiner here, I think, once again pointed to a specific
17 formulation of Desonide at a certain percent and said, you know, this is
18 termed to be a low or medium-strength formulation. However, because
19 these are anhydrous formulations which are always going to be higher
20 potency, so you're already looking at a medium to medium-high to begin
21 with, and on top of that you now have a penetration enhancer which is going
22 to increase penetration of the steroid into the dermis and the epidermis,
23 you're more likely to get side effects, the local side effects that we're trying
24 to avoid.

25 JUDGE SCHEINER: Is there anything of record that supports your
26 statement that the anhydrous formulations are typically, or—

1 MR.TERAPANE: Sure. Actually, if you look in the Quigley, that
2 table in Quigley—

3 JUDGE SCHEINER: Okay. I mean, oh, okay, but have you
4 discussed that on the record?

5 MR. TERAPANE: I know we have, we do have some discussion in
6 the Appeal Brief and in the Reply Brief about the fact that the potency
7 differs based on the formulation, the vehicle carrier.

8 JUDGE SCHEINER: Okay.

9 MR. TERAPANE: I don't know if that specific point was made, but
10 we certainly talked about the fact that when you go from lotion to cream to
11 ointment, those potencies are going to differ because of the carrier vehicle.

12 JUDGE WALSH: Okay.

13 MR. TERAPANE: And like I said, even within the same carrier
14 vehicle, within various creams or lotions or ointments, you're going to get
15 different potencies as well.

16 So with respect to Burnett, I really think that's the main point that we
17 want to make here, is that you have an ointment which is anhydrous, which
18 is going to increase potency, in combination with a penetration enhancer
19 which is going to increase potency because it increases absorption of the
20 steroid into the dermis and the epidermis. And, therefore, you're more likely
21 to get the local side effects that we're trying to avoid. And once again, no
22 explicit teaching here of using a low or low-to-medium strength potency
23 steroid formulation to treat a fungal infection like we're claiming.

24 Any questions on Burnett?

25 JUDGE SCHEINER: No.

26

1 MR. TERAPANE: Okay. Then the Examiner made an obviousness
2 rejection over Quigley by itself. I'm not sure I need to add much more.

3 JUDGE SCHEINER: No.

4 MR. TERAPANE: And I addressed, I think, the question you had
5 raised with respect to obviousness in that certain passage. So, certainly, the
6 arguments we made previously apply here. Once again, we think the focus
7 here is really on, at best medium, but more likely a medium-high to high-
8 potency formulation based on not only the prophetic examples but the
9 working examples.

10 The second obviousness rejection was with respect to Burnett in
11 combination with Shah. We've talked about Burnett and the issues that we
12 think are there. The Examiner cited Shah for a specific purpose which is -- I
13 think, according to him, he cited it because he wanted it to provide some
14 other antifungal compounds that weren't explicitly disclosed in the Burnett
15 reference. However, he sort of ignored the rest of the disclosure.

16 First of all, Shah is also a composition containing a penetration
17 enhancer, so you're going to be increasing, once again, absorption of the
18 steroid and, therefore, increasing the potency. But also, Shah specifically
19 teaches at columns, excuse me, at the top of column 4 -- this is starting at
20 line 3 -- that mid-potency steroids are preferred in that reference, because
21 there are problems with either strong or -- and low-potency steroids. So if
22 you were going to combine these two references, and you have to consider
23 the references as a whole, which the Examiner did not do here -- if I'm
24 combining Shah with Burnett, what I'm doing is I'm making a formulation
25 that contains a mid-potency steroid with a penetration enhancer, which
26 means I'm going to end up increasing the potency, ultimately, of it to maybe

1 medium-high, based on the fact that it's going to be absorbed deeper into the
2 skin. But once again, there's nothing here to support choosing a low to low-
3 medium potency steroid as a means for effectively treating a fungal infection
4 while avoiding, you know, the local side effects that we're trying to avoid.

5 JUDGE WALSH: Mr. Terapane, you said that the -- had two
6 comments on your arguments about the first. The Examiner pointed out that
7 Burnett and your claims both -- and second, the Examiner argues over a
8 claim interpretation of Claim 1, at the wherein clause. The Claim reads
9 "The composition does not put -- had caused undesirable local side effects."
10 The Examiner took the opinion that one could have a composition with
11 steroids to penetrate the skin, but they don't cause undesirable side effects,
12 and that that would be -- would you comment on those two points?

13 MR. TERAPANE: Sure. So I think with the first, with respect to the
14 propylene glycol comment that he made, there's a very telling passage, and
15 this is in Shah once again, at the bottom of column 2, starting at line 65,
16 which says "It is well known that the effectiveness of a penetration enhancer
17 depends on the type of drug molecule and the composition of the
18 formulation."

19 So what that means is, just because we may say that propylene glycol
20 could be a solvent in a particular formulation, doesn't mean it acts as a
21 penetration enhancer, because the effectiveness of something to be a
22 penetration enhancer depends on the drug that you are formulating, but also
23 what other components are in that formulation. Matter of fact, Shah says
24 specifically, you can see serious drop-off in the effectiveness of enhancing
25 penetration as you start adding multiple components to the composition.

26

1 So I think that's -- it's a bit of a red herring in the sense that he really
2 took it out of isolation and said, okay, if you've got PG and they've got PG,
3 it's got to be the same thing. That's not it at all. You've got to look at the
4 specific formulation, what else is there, what the drug is, and whether or not
5 what you're using actually acts as a penetration enhancer. Not to mention
6 most of the time, PG is also used in combination with other materials to
7 enhance penetration. So that would be my counter with respect to that.

8 With respect to his interpretation of the Claim, I'm not sure that I
9 exactly followed the point that he was trying to make. I mean, I think when
10 you have a topical fungal infection, it's going to be located primarily on the
11 skin, it's going to be somewhat into the skin, and so no matter what
12 formulation you apply, you're going to get some absorption into the skin.

13 What we're trying -- you know, what we're claiming and what this
14 composition is designed to do is to minimize that absorption into the skin so
15 that you don't get those local side effects that you see with the high-potency
16 formulations. And so I think, you know, to distinguish us from the prior art,
17 I mean the prior art really said, we are trying to get this into the skin, that's
18 what we're trying to do; we want it deep into the dermis and the epidermis.

19 Well, that's fine. I mean it gets you in contact with the fungal
20 infection. However, because you are starting with a, excuse me, with a mid-
21 potency steroid, or even a high potency steroid, you now have this very
22 strong active agent in the skin which then gives rise to these local side
23 effects, which is, as Dr. Goldstein's going to attest to, are in some ways
24 worse than the actual underlying fungal infection in terms of the symptoms
25 that the patient is suffering from.

26

1 And so I'm not sure I understand the point he's trying to make, but I
2 think we've clearly distinguished that the references that have been cited
3 versus what we're claiming.

4 JUDGE WALSH: Thank you.

5 MR. TERAPANE: Okay. How much time do we have?

6 JUDGE SCHEINER: Just a few minutes.

7 MR. TERAPANE: Okay. He only needs maybe, probably, three to
8 five minutes tops --

9 JUDGE WALSH: Okay, Dr. Goldstein.

10 MR. TERAPANE: So, okay. Thanks.

11 DR. GOLDSTEIN: Good morning, Your Honors.

12 JUDGE SCHEINER: Good morning.

13 DR. GOLDSTEIN: My name's Jay Goldstein; I'm a dermatologist,
14 I've been in practice for 30 years. Tinea, or a fungus, or ringworm is one of
15 the more common things we see in practice. It presents usually as red, scaly
16 areas on the skin, often associated with a lot of itching, and so severe it can
17 keep patients up at night.

18 At the time of our filing in 2002 or so, the way of treating fungal
19 infections was twofold: one is by the use of an antifungal alone; and the
20 second was with the use of an antifungal with a high-potency topical steroid.
21 This was known as Lotrisone; it was a combination of betamethasone
22 dipropionate, which is a high-potency class I or II steroid in association with
23 an antifungal.

24 The problem with treating only with an antifungal is that it doesn't
25 alleviate the itching or pruritus in the patient until the fungal infection clears,
26 which can be in the neighborhood of four to six weeks, if not longer. So

1 although you're, effectively, treating the fungus; the symptoms continue, the
2 patient is still miserable, there's still scratching. So they added the topical
3 steroid, betamethasone dipropionate, which is a Class I or II, to try to
4 alleviate the itching from the fungal infection, and they found that the fungal
5 infection actually did clear somewhat quicker.

6 The problem is the terrible side effects which can happen from the
7 usage of the high-potency topical steroid. The ones we usually see are what
8 are called striae distensae, which are basically stretch marks, and they can
9 last forever. They're extremely unsightly, they are impossible to treat.
10 Sometimes your body clears, though more often they don't.

11 So in some ways, the usage of Lotrisone, although effective for the
12 tinea or the fungal infection, the treatment was worse than the disease
13 because the patients wound up with striae distensae, so much so that the
14 American Academy of Pediatrics put out an advisory that Lotrisone should
15 not be used in the pediatric age group because of the side effects of the striae
16 distensae.

17 So at the time I was thinking, myself, that perhaps if we lowered the
18 potency of the cortisone of the steroid cream to a low to a low-medium
19 potency, we would still get efficacy in terms of treating the tinea, or fungal
20 infection, and also we would decrease the itching to a significant degree so
21 the patients would clear just as quickly as with the high-potency steroid.

22 So what I did is, I took my patients who had significant tinea or fungal
23 infections, and I had them use a standard antifungal, and I had them use a --
24 and we used alongside with it, in a formulation, a low potency, low to low-
25 medium potency steroid, and we made -- we used several different types of
26 steroids, we used several different types of antifungals. And, surprisingly,

1 they all worked. They worked beautifully. The patients were thrilled, the
2 itching went way down, inflammation went way down. And the best news,
3 of course, was that there were absolutely no side effects, and I mean zero
4 side effects. There was no striae distensae or stretch marks, there was no
5 hypopigmentation. So I was thrilled with the results, and we continue to use
6 it in my office to this day.

7 So that was the nature of my invention, that I figured, I hoped counter
8 intuitively, that if we lowered the cortisone, the steroid strength, we would
9 still get the advantages of the higher-potency steroid without the severe side
10 effects, and that's exactly what happened. Thank you.

11 JUDGE SCHEINER: Thank you.

12 DR. GOLDSTEIN: Okay. Thank you.

13 JUDGE SCHEINER: Do you have anything further? Judge Walsh,
14 can you hear me?

15 JUDGE WALSH: No questions. Thank you.

16 MR. TERAPANE: Okay.

17 JUDGE SCHEINER: I'm not used to this.

18 MR. TERAPANE: No. I understand. It's new for us as well, so --

19 JUDGE SCHEINER: Do you have anything further?

20 JUDGE GREEN: No.

21 MR. TERAPANE: Okay.

22 JUDGE SCHEINER: Well, thank you for coming in. I think we
23 understand the issue.

24 MR. TERAPANE: Thank you for your time, we appreciate it.

25 JUDGE SCHEINER: And thank you for your explanations.

26 MR. TERAPANE: Okay, thank you.

1 DR. GOLDSTEIN: Thank you.

2 MR. TERAPANE: Thank you very much.

3 DR. GOLDSTEIN: Judge, thank you.

4 MR. TERAPANE: Have a good day, thank you.

5 JUDGE SCHEINER: Thank you.

6 DR. GOLDSTEIN: Thank you.

7 (Whereupon, the proceedings, at 9:25 a.m., were concluded.)

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